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Use of antidepressant medications not associated with A1C among individuals with diabetes in NHANES sample

Jamie Kammer, Akiko S. Hosler**, Emily Leckman-Westin, A. Gregory DiRienzo*

State University of New York at Albany, Department of Epidemiology and Biostatistics, School of Public Health, One University Place, Rensselaer, NY 12144, United States

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ABSTRACT

Introduction: Studies on the relationships between antidepressant medications and A1C, a measure of glucose levels over the past three months, have resulted in mixed findings. Most available research examined subclass effects. The current study aims to measure the association between individual antidepressant medications and A1C in a large nationally-representative dataset.

Methods: The sample of this study consists of 45,786 individuals who participated in the National Health and Nutrition Examination Survey between 1999 and 2012. We examined the relationships between 18 antidepressant medications and continuous A1C in crude and adjusted linear models stratified by diabetes status (ever or never diagnosed). Adjusted models included demographic covariates (age, gender, race/ethnicity, and education), smoking status, and physical activity.

Results: No significant associations were found for most antidepressants. However, those who used selegiline ($n = 11$), all of whom were in the no diabetes stratum, were found to have a higher A1C compared with individuals who do not use antidepressants.

Discussion: The study agrees with a number of earlier findings. Most antidepressant medications do not appear to be associated with A1C levels among individuals with or without diabetes. Limitations include small numbers for some exposure categories and cross-sectional data. Strengths include use of a nationally-representative dataset and large total sample size.

* *Corresponding author*. Tel.: +1 518 549 5181.
** *Corresponding author*. Tel.: +1 518 402 1561; fax: +1 518 402 0380.
E-mail addresses: JKammer@albany.edu (J. Kammer), ahosler@albany.edu (A.S. Hosler).

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1. Introduction

The proportion of individuals who take an antidepressant has increased in recent years [1]. It is estimated that more than one in ten individuals in the United States over the age of 12 currently take an antidepressant medication and the majority have been taking them for at least two years [2]. Given the high prevalence of their use, it is important to understand the impact each of these medications may have on other health outcomes, especially those related to already prevalent conditions, such as diabetes. While evidence suggests that another class of psychotropic medications, antipsychotics, can lead to poorer cardiometabolic health outcomes, including diabetes and worse glycemic control [3–6], the effects that antidepressants may have is less well-understood.

A number of studies have attempted to examine the association between antidepressants and diabetes and findings have been mixed. Importantly, a recent article by Kivimaki and Batty [7] highlighted the fact that these studies can suffer from ascertainment bias when the outcome is measured using self-reported diabetes diagnosis. Therefore, it is important to use glucose levels or other biomarkers in investigating potential medication effects. However, this does not completely explain extant findings, as some prospective studies have also found antidepressant use to be associated with increased diabetes risk when defined by glucose levels. For example, in a large cohort of individuals with impaired glucose tolerance, Rubin [8] found that those who used antidepressants were more likely to experience subsequent diabetes as measured by a blood glucose test.

In measuring the effects of antidepressants on chronic disease outcomes, it is also important to differentiate between subclass categories, as biological mechanisms may differ. A meta-analysis published within the past few years by Yoon [9] found that both selective serotonin reuptake-inhibitors (SSRIs) and tricyclic antidepressants (TCAs) were associated with an increased risk for diabetes. However, a review by Deuschle [10] suggests that these two subclasses may have divergent effects, with TCAs worsening glucose control. In another review of the literature, McIntyre [11] attempted to explore the mechanisms behind some of the observed associations in addition to examining the relationships between specific antidepressant subclasses and diabetes outcomes. In this study, the authors concluded that the syntheses of preclinical and clinical studies indicate that noradrenergic antidepressants reduce insulin sensitivity while serotonergic antidepressants increase insulin sensitivity and glucose storage. Lastly, the authors report on evidence from multiple studies showing that monoamine-oxidase inhibitors (MAOIs) lower blood glucose levels. In another review, Barnard [12] also found that noradrenergic antidepressants were associated with poorer glycemic outcomes. However, in this study the authors highlighted the fact that more recent and larger studies found only modest associations between antidepressants and glycemic outcomes. Importantly, they also note that few studies differentiate between antidepressant agents within subclasses and express the need for more insight into specific associations as even within subclasses antidepressant effects may differ. For example, differences in effects on weight gain were observed among those who used paroxetine and sertraline, both of which are SSRIs [13].

A review of available studies that have examined the association between specific antidepressant medications and continuous A1C, a measure of glucose levels over roughly the prior three months, indicates that potential glycemic effects have not been well-investigated for a large number of antidepressant medications, and this is especially the case for individuals who are not already diagnosed with diabetes. It is important to study associations in those with and without diabetes separately as effects may be more pronounced or may only exist among those with poorer glycemic response. Furthermore, taken together, the results of studies that have examined this question show that medications within the same subclass can have divergent effect on glycemic outcomes. For example, studies to date have shown no association between paroxetine and A1C while some evidence points to a negative association with sertraline [14–18]. The aim of the present study is to quantify the associations between individual antidepressant medications, many of which have not had their potential glycemic effects previously studied, and continuous A1C stratified by diabetes status.

2. Methods

2.1. *Participants*

The National Health and Nutrition Examination Survey (NHANES) Continuous is a project of the Centers for Disease Control and Prevention (CDC) that collects health data including demographics, risk factors, health behaviors, and other information from a representative sample of about 5000 individuals in the United States every year [19]. Subsets of interviewees also participate in a medical exam and provide laboratory samples. Those 12 and over are eligible to provide blood samples. Data from the NHANES is used to provide information on the health of the U.S. population and inform public health program planning. NHANES Continuous data collection has been ongoing since 1999 and data is made publicly available and can be accessed through the CDC website [19].

A total of 45,786 with complete A1C, antidepressant exposure, demographic, and diabetes diagnosis data who participated between 1999 and 2012 were included in the present study. Three-thousand and seventy individuals in the original sample had missing A1C information. Another 74 with A1C available were missing data for the item on whether or not medication was taken in the past 30 days and another 78 with non-missing A1C and medication information were missing covariate information for at least one demographic variable (age, sex, race, education) or diabetes diagnosis for a total of 3222 (6.57%) individuals missing data for at least one variable who were left out of univariate and bivariate analyses in the crude and demographics-adjusted models. Those on antidepressants used by less than 10 people and those on combination agents (33 individuals) were also excluded from analyses. Further analyses were conducted in samples of individuals who also had complete data on smoking status ($N = 33{,}969$) and physical activity ($N = 33{,}961$).